REMARKS

Amendment and Status of the Claims

In the Advisory Action dated June 1, 2010, the Examiner indicated that the claim amendments presented in the Amendment and Response filed February 8, 2010, had been entered. Therefore, the amendments herein are shown relative to the claims as pending after the entry of the amendments presented in the Amendment and Response filed February 8, 2010.

Claims 76, 78, 80, and 83 have been amended to more particularly point out and distinctly claim certain subject matter. Support for the amendments can be found throughout the specification, e.g., at page 5, lines 6-22. No new matter has been added.

Now pending in the application are claims 62-63, 66, 69-76, 78-80, and 82-83.

Rejections under 35 U.S.C. §112, second paragraph

Applicant thanks Examiner Padmanabhan for the courtesy of a telephonic interview conducted on April 6, 2010, with the undersigned representative (the "Interview"). At the Interview, the status of the claims and the finality of the Office Action were discussed. No final agreement was reached.

Rejections under 35 U.S.C. §112, second paragraph

(i) Claims 76-80 and 82-84 were rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite "because it is uncertain as to if medicaments are referring to separate formulations, respectively or medicaments in a concomitant formulation." This rejection is traversed.

Without agreeing with the rejection, Applicant notes that claim 76 has been amended to recite that the medicament consists of (i) a first formulation comprising an antidepressant formulated for nasal administration; and (ii) a second formulation comprising an antidepressant formulated for local administration to at least part of the male genitalia. Applicant contends that this language is clear and is not indefinite.

(ii) Claim 73 was rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite. This rejection is traversed.

Without agreeing with the rejection, Applicant notes that claim 73 was previously amended to recite that the antidepressant is massaged into the skin of the male genitalia for about one minute prior to intercourse, i.e., as suggested by the Examiner. Applicant contends that this language is clear and is not indefinite.

Reconsideration and withdrawal of the rejections is proper and the same is rejected.

Rejection under 35 U.S.C. §102(b)

Claims 76, 77[1], and 79 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Altabet (U.S. Patent No. 6,943,193, hereinafter "Altabet"). This rejection is traversed.

A reference anticipates a claim only if the reference discloses "each and every element as set forth in the claim." MPEP 2131. Although the Office Action asserts that Altabet "teaches atomoxetine . . . formulations for administration by nasal, transdermal (i.e., skin patch), and percutaneous, intravenous, intramuscular or intrarectal delivery", the Office Action does not allege that Altabet teaches administration of atomoxetine, or any other antidepressant, by a combination of two or more routes of administration that act synergistically.

The Advisory Action states that "Altabet clearly anticipates the invention . . . administering an agent via two or more modes of administration is well-established." This statement is traversed. Altabet does not teach or suggest a medicament consisting of a first formulation comprising an antidepressant formulated for nasal administration; and a second formulation comprising an antidepressant formulated for local administration to at least part of the male genitalia. Neither the Office Action nor the Advisory Action even alleges that Altabet discloses any such combination. Applicants respectfully submit that Altabet does not disclose each and every element of the present claims, and therefore does not and cannot anticipate the pending claims.

[1] Applicants note that claim 77 has been cancelled. Applicants further understand that the Office Action may have intended to reject claims 80, 82, and 83 as anticipated by Altabet. Such a rejection of those claims is traversed for at least the reasons described herein.

Reconsideration and withdrawal of the rejection is proper and the same is rejected.

Rejection under 35 U.S.C. §103(a)

(i) In the Office Action, claims 62, 63, 66 and 69-75 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Bar-Or (U.S. Patent Publication No. 2002/0132857, "Bar-Or") in view of Crenshaw et al. (U.S. Patent No. 5,151,448, "Crenshaw") and Rojas-Corrales et al. (J. Psychopharmacol. 18(3):404-411 (2004), "Rojas-Corrales"). This rejection is traversed.

According to the Office Action, Bar-Or "teaches that formulations were known in the prior art using anti-depressants . . . The combination of any known effective antidepressants would have been obvious in view of Kerkhoven." Applicant cannot agree. Bar-Or teaches tramodol, but it is clear from the context that, according to Bar-Or, oral dosage, i.e., a single use, is preferred. Bar-Or does not teach or suggest administration of (i) an antidepressant formulated for nasal administration; and (ii) an antidepressant formulated for local administration to at least part of the male genitalia, as required by the pending claims.

Crenshaw does not remedy the deficiencies of the Bar-Or reference. Crenshaw teaches that premature ejaculation in male humans patients can be effectively treated by the administration, preferably oral, of a fluoxetine dose effective to delay the onset of ejaculation during subsequent sexual intercourse (see, e.g., column 1, lines 49-52). As recited again at column 1, lines 59 and 59, oral administration is preferred. Crenshaw does not teach administration of an antidepressant by nasal administration, nor (as the Office Action appears to concede) does it teach the combination of (i) an antidepressant formulated for nasal administration; and (ii) an antidepressant formulated for local administration to at least part of the male genitalia, as presently claimed. Indeed, Crenshaw does not teach any form of administration other than administration via a single route, in which administration is preferably oral administration.

Rojas-Corrales is cited only to show that tramodol has anti-depressant activity. However, Rojas-Corrales does not remedy the deficiencies of Bar-Or and Crenshaw. Rojas-Corrales does not teach or suggest the combination of (i) an antidepressant

formulated for nasal administration; and (ii) an antidepressant formulated for local administration to at least part of the male genitalia, as presently claimed.

None of Bar-Or, Crenshaw, or Rojas-Corrales discloses or suggests administration of an anti-depressant or anti-depressants by a specific combination of routes, and one of ordinary skill in the art would not have been motivated to modify the teachings of the references to arrive at the subject matter of the present claims. Moreover, none of the references teaches or suggests that synergistic results can be obtained by administration of anti-depressants in a specific combination as presently claimed. Applicant therefore submits that the claims are not render unpatentable by the teachings of Bar-Or, Crenshaw or Rojas-Corrales, whether taken alone or in combination.

(ii) In the Office Action, claims 78, 80, 82, 83 and 84 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Bar-Or (U.S. Patent Publication No. 2002/0132857, "Bar-Or") in view of Crenshaw et al. (U.S. Patent No. 5,151,448, "Crenshaw") and in further view of Rojas-Corrales et al. and further in view of Bodor U.S. Patent No. 5,024,998, "Bodor"). This rejection is traversed.

The Office Action concedes that none of Bar-Or, Crenshaw or Rojas-Corrales, alone or in combination, teach "a medicament comprising of a serotonin reuptake inhibitor and MAO-inhibitors." However, the Office Action states that Bodor teaches "that the cyclodextrin complexes of the invention are preferably administered in the form of a pharmaceutical composition" that can be administered by "oral, buccal, sublingual, topical . . . rectal, vaginal, nasal, and parenteral" routes of administration. The Office Action concludes that "it would have been apparent and prima facie obvious to the one of skill to optimize the characterization of such therapy to achieve satisfaction and/or the desired effect." Applicant cannot agree.

The teachings of Bar-Or, Crenshaw and Rojas-Corrales have been discussed above. As Applicant understands the reference, Bodor is concerned with alleviating the problem of precipitation of drugs at or near and administration site (see Bodor, e.g., the "Objects of the Invention"). Bodor is thus directed to problems of formulation rather than to providing compositions that, appropriately combined, can address the problem

of premature ejaculation with unexpected therapeutic benefits. Bodor therefore does not remedy the deficiencies of Bar-Or, Crenshaw and Rojas-Corrales. Accordingly, none of the references, taken alone or in any combination, can render obvious the claimed subject matter.

Furthermore, even if a prima facie case of obviousness had been made out in the Office Action (which Applicant strongly disputes), Applicant has shown that the administration of an antidepressant via a combination of nasal administration and administration to at least a part of the male genitalia as presently claimed, can significantly improve the time to ejaculation, which is otherwise not achievable when the antidepressant is administered via only one route of administration.

As discussed in the response filed May 11, 2009, and as disclosed in the present specification, the Applicant has surprisingly found that by splitting the routes of administration, an increased level of satisfaction is experienced by patients suffering from premature ejaculation. The symbol ++ in the table at page 15 of the specification relates to a measure of satisfaction, which is not a quantitative measure. It is believed (without wishing to be bound by theory), based upon clinical observation, that by splitting the routes of administration, the medicament can absorb rapidly into the central nervous system and, at the same time, act on the nerve endings in the penis to provide partial desensitization. This effect is otherwise not achievable if the antidepressant is administered via only one route. This is neither taught nor disclosed in the cited prior art. This effect is also unexpected and unpredictable.

Although the Office Action states that "[t]he Table at page 15 provides no data of both statistical and practical significance upon which to base a conclusion of superiority of the claimed methods", Applicant cannot agree. Given the nature of the study discussed above, the data is necessarily qualitative. For example, the "++" result on the table at page 15 of the specification is not the result of a purely additive effect for, e.g., administering twice the amount of the active compound(s), but rather is a result of administering the antidepressant by a <u>combination</u> of different routes. Further, the claimed methods and medicaments achieve the desired result of reducing premature ejaculation by using a lesser quantity of the antidepressant via each route, as the total quantity of antidepressant is administered via a combination of two (or more) routes.

Applicant further notes that claims 62 and 76 (from which the remaining claims depend, either directly or indirectly) recite that the concentration of each antidepressant is between 1 to 10% by weight.

Furthermore, the Examiner should "consider all rebuttal arguments and evidence presented by applicants." MPEP 2145. Applicant submits that the Office Action unduly disparages the evidence provided. For instance, the Office Action states that "there is no assessment of what positive psychological effect the simple act of self-administering the compositions by the ++ group contributes to the outcome." However, Applicant points out that the ++ group can be compared to the other groups, in which only a single route of administration (nasal, buccal, or pulmonary) was used. The combination of nasal and topical administration was seen to be more satisfactory than any of the single routes. The Office Action provides no evidence that the "positive psychological effect [of] the simple act of self-administering the compositions" is different for the various groups, and Applicant submits that the proffered evidence should be given appropriate weight and not simply dismissed, as the Office Action appears to do.

(iii) In the Advisory Action, claims 62, 63, 66, and 69-75 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Bar-Or (U.S. Patent Publication No. 2002/0132857, "Bar-Or") in view of Crenshaw et al. (U.S. Patent No. 5,151,448, "Crenshaw") and Bodor, U.S. Patent No. 5,024,998, "Bodor"). This rejection is traversed.

The Advisory Action states that "Bodor teaches contemplated routes of administration which are both vaginally and nasally . . . Bodor establishes the motivation as to why one of skill would instantly recognize that more than one route of administration in view of the nature of the drug is essential in comprehensive treatment for the disorder." Applicant respectfully contends that this is incorrect. At the table bridging columns 5 and 6, footnote 2 to the table, Bodor refers to a prior art document which references, "nasal, vaginal or rectal" administration. However, the routes are clearly given as alternatives, not as any combination. As Applicant understands the Bodor reference, Bodor does not refer to combinations of routes of administration,

much less cause one of skill in the art to "instantly recognize that more than one route of administration . . . is essential."

Further, the Advisory Action states that "in the context of the claimed invention, the male genitialia [sic] could be interchanged with the term vagina." Applicant cannot agree. In the context of the presently-claimed method of treating premature ejaculation in a male, the male genitalia cannot be "interchanged with the term vagina." Nothing in Bodor teaches or suggests administration to at least a part of the male genitalia, as required by the present claims. As noted above, nothing in Bodor teaches or suggests administration by a combination of routes of administration, as required by the present claims.

Applicant respectfully contends that the cited references cannot render obvious the present claims, whether those references are taken alone or in any combination. Reconsideration and withdrawal of the rejections is proper and the same is requested.

CONCLUSION

For at least the foregoing reasons, all claims of this application are deemed to be in condition for allowance, and allowance is accordingly requested. However, if the Examiner considers that obstacles to allowance remain, the Examiner is invited to contact the undersigned.

Applicant requests any extension of time necessary for consideration of this response. If for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. **04-1105**, under Reference No. 64734 (70403), Customer No. 21874.

Dated: August 6, 2010

Respectfully submitted,

By: /Mark D. Russett/
Mark D. Russett, Reg. No.: 41,281
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 239-0100
Attorneys/Agents For Applicant